Attorney Docket No. (P3250) 6675.142US1 Serial No. 09/359,260

Remarks

In response to the Notice of Non-Compliant Amendment dated November 30, 2004, Applicant submits herewith a complete listing of the claims (claims 1-134) for the present application. Applicant requests that the documents filed on September 10, 2004, along with the present filing, now be considered by the Examiner.

By the present Amendment, claim 74 and 77-81 have been cancelled, and claims 76, 82-89, and 91-95 amended. Claims 128-134 are newly presented for consideration. Accordingly, claims 76, 82-95, and 128-134 are now pending in the application.

In the Office Action of July 15, 2003, claims 74 and 76-95 were rejected under 35 U.S.C. §101 and 112, first paragraph for lack of utility. Claims 74 and 76-95 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. Claims 74 and 76-95 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claims 74, 81, 87-90, and 94 were rejected under 35 U.S.C. §102(b) as being anticipated by Tenson, et al. Claims 74, 92, 94, and 95 were rejected under 35 U.S.C. §102(b) as being anticipated by Ostrem. The cancellation of claims 74 and 76-80 renders some of these grounds of rejection moot. With respect to the pending claims, these rejections are respectfully traversed.

I. Support for Claim Amendments

Claims 128-134 have been introduced to more clearly define the invention by addressing, at least in part, some of the issues of indefiniteness raised in the Office Action, and to secure additional coverage for subject matter to which Applicants are entitled protection. Amendments have also been made to reflect proper dependency and also address some of the issues of indefiniteness raised in the Office Action. Applicants respectfully submit that the new and amended claims are fully supported by the specification. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

II. Utility Rejection of Claims 74 and 76-95 under 35 U.S.C. §§ 101 and 112, ¶1

The Examiner has rejected claims 74 and 76-95 under 35 U.S.C. §§101 and 112, ¶1 because the claimed invention allegedly is not supported by either a specific asserted utility or a well-established (real-world) utility. According to the Examiner, the specification provides only exploratory studies and theories without describing a single peptide having a specific utility. The Examiner states that the specification's stated intended uses, such as drug discovery, identifying components of culture medium, and identifying and/or designing peptides with particular pharmacological or therapeutics activities, are not "specific uses". In addition, the Examiner urges that there is no immediately apparent (real-world) utility because there is no well-established use of the library or a correlation between the claimed library and a disease or disorder.

The claims are directed to a screening method, which is used to assist a researcher in the identification of a peptide that possesses a desired characteristic. This screening method uses qualitative and/or quantitative data from the test compounds to identify appropriate sets of candidate compounds having a particular activity as determined by the user. Applicants submit that one skilled in the art would readily appreciate that this invention has specific, substantial, and a real world utility.

At the outset, applicants submit that the PTO has the initial burden to establish the presumptively correct assertion of utility in the disclosure. *See* MPEP 2107 ("Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a

statement.") The instant utility rejection fails to provide any evidence that would suggest that the utilities stated therein are not true.

The Examiner argues that "only after further research and further experiments" would the claimed invention be made useful. Applicants acknowledge that the claimed invention is typically used in a laboratory setting. However, contrary to the Examiner's assertion that this itself constitutes a lack of utility, the Utility Guidelines specifically provides that "[m]any research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds)". MPEP 2107.01. Moreover, the Utility Guidelines go on to negate the Examiner's assertion noting that "[a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact 'useful' in a patent sense." MPEP 2107.01. Applicants herein contend that the claimed process has a specific and real world utility, such as to reduce the amount of experimentation necessary to identify useful peptides in research settings.

The Examiner has not set forth any reason, other than being a research tool, that the claimed method lacks utility. Applicants, on the other hand, have described the method of identifying candidate peptides, as claimed herein, as having a specific and real world utility, *e.g.*, to analyze a group of compounds having a desired activity, using qualitative and/or quantitative data about those compounds. The Examiner rejects the claimed method stating that not a single peptide has been identified with a specific utility. However, applicants respectfully submit that unknown, unidentified peptides *per se* are not herein claimed. Rather, the claims are directed to a method to assist researchers to identify and pre-select suitable candidates peptides that satisfy a particular test requirement, a utility that any person skilled in this art would appreciate.

The specification describes this process. For example, at page 31, the specification describes the use of eight test peptides and the identification of three parameters, hydrophobicity, molecular weight, and total charge. In this example, the biological activity (such as protein production) represents the indicia of activity. Using this quantitative information (qualitative information may also be used), a mathematical equation is developed to define the relationship between these three values as set forth in the equation on page 32 representing the relationship between the three values of hydrophobicity (first parameter), molecular weight (second parameter), and biological activity (indicia of activity). The identification of this relationship between these three values, as used in this example, permits the user of the invention to then develop another set of peptides. For example, the specification describes the use of the mathematical equation on page 32 to predict the biological activity for an untested peptide, HYPV. Specifically, a biological activity of 28.2 was predicted for the untested peptide HYPV using only its hydrophobicity and molecular weight based on the mathematical equation. If the test requirement requires a predicted activity of at least 25, then the HYPV peptide represents a good candidate for further synthesis and testing. If, on the other hand, the test requirement requires a predicted activity of at least 30, then the screening process would continue.

Other examples are provided in the specification to establish other types of relationships that may be developed using the first and second parameters and indicia of activity to aid in the identification of suitable candidates. For example, quantitative structure-activity relationships (p. 30), conventional line-fitting algorithms (p. 33), and distance function relationships (p. 34) can be suitably used with the present invention.

In addition, applicants need only describe a single specific, substantial utility. The specification provides that the claimed invention can be used in drug discovery, identifying

suitable components in a culture medium, or identifying peptides having pharmacological or therapeutic activity. However, the Examiner has not pointed to any specific reason why such utilities are not to be believed. Rather, research tools, including screening assays, such as that claimed herein, have been previously patented acknowledging the skilled artisan's appreciation for the utility of the claimed invention. For example, a method of identifying probes to quantify the quantitative expression of a target nucleic acid was patented in U.S. Patent No. 6,548,257; a method for identifying one or more compounds that modulate the formation of complexes including a first test member and a second test member was patented in U.S. Patent No. 6,664,048; and a method for detecting interactions between one or more compounds and one or more protein-nucleic acid fusions was patented in U.S. Patent No. 6,602,685.

While the steps of the process require that the skilled artisan be capable of defining the relationship between the first and second parameters and the indicia of activity, applicants respectfully submit that this does not constitute "carrying out further research to identify or reasonably confirm a 'real world' contest of use" to preempt a finding of specific, substantial utility. In fact, if this were true, no patents relating to bioinformatics would conform to the patentability standards held by the Examiner. Instead, the court has specifically held that the "threshold of utility is not high: An invention is "useful" under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966) Applicants respectfully contend that ample information has been provided to allow the skilled artisan to practice the claimed invention in order to demonstrate its utility and that the specification describes how to practice the claimed invention. One skilled in the art and specifically, skilled in the identification of suitable

parameters and identification of correlating relationships between such parameters, would readily appreciate the utility of the claimed method.

In fact, applicants have used the claimed method to identify peptides in a variety of applications. For example, in U.S. Application No. 09/992,124 (U.S. Publication No. US 2003/0162289)("the '124 application"), a copy of which is attached for the Examiner's convenience, applicants used the claimed method to identify peptides affecting cell adherence and growth (*see* Examples 1-5) as well as those affecting secretion of platelet derived growth factor (PDGF)(*see* Examples 6-11). Paragraph No. 32 of the '124 application indicates that these peptides were characterized by their whole molecule parameters such as charge, molecular weight, and mass, as well as by their sequence-specific parameters such as hydrophobicity and polarity of their side chains. The initial libraries were screened for cell adherence and growth (based on an increase in oxygen consumption of the culture cells) or their affects on PGDF secretion (based on supernatant levels of PDGF through a sandwich ELISA). Using this information and through the identification and analysis of these characteristics relative to their cell adherence and growth or PGDF secretion, applicants established that a "Nearest Neighbor" relationship was most appropriate for this particular application. (*See* '124 application, Paragraph No. 31.) Using the test requirement set by applicants, candidates were identified. Example 5 describes the candidates that affect cell adherence and growth and Example 10 describes the candidates that affect secretion of PGDF. Therefore, applicants have provided the information necessary to prevent the practice of the claimed invention as a "guessing game," and instead have described each step of the claimed method to allow one to use and practice the invention.

Nevertheless, in order to further prosecution of the instant application, applicants have deleted claim 74 and added new claim 128. Claim 128 recites a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The claimed method comprises constructing a first test peptide library comprising a plurality of first test peptides by means of a space-filling design, wherein the length of said first test peptides comprises no greater than twenty amino acids, and wherein said first test peptides are characterized by a first parameter and a second parameter. The first parameter is a whole molecule parameter and the second parameter is a sequence-specific parameter. An activity having a first indicia is determined and measured in the plurality of first test peptides. The claim then recites that the relationship between the first indicia of the activity, the first parameter, and the second parameter is determined. The estimated first indicia for each candidate peptide is then calculated using the determined relationship. A test requirement is set, based on a desired activity, having a test indicia range. Next, a second test peptide library is created containing at least one second test peptide. The at least one second test peptide comprises candidate peptides having an estimated first indicia that satisfies said test requirement. The first indicia of the at least one second test peptide is determined in order to identify at least one second test peptide having a first indicia that satisfies the test requirement. Applicants respectfully submit that this new claim reflects the claimed screening utility as represented and adequately enabled in the present invention.

Therefore, the use of the qualitative and/or quantitative information of the test compounds to screen for suitable candidate peptides, as identified by applicants, described in the specification, and claimed herein, is a specific, real world utility used to identify candidate peptides having desired activities.

III. Rejection of claims 74 and 76-95 under 35 U.S.C. § 112, first paragraph

Claims 74 and 76-97 are rejected under 35 U.S.C. §112, first paragraph, as the specification allegedly fails to adequately describe the claimed subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. The Examiner contends that the specification does not identify a peptide with an activity that satisfies a test requirement. The Examiner states that the "generalized statements" and definitions are "not very descriptive' or "art-recognized." Instead, the Examiner states that the methods are "exploration by trial and error to find a peptide having a desired activity, if any." The Examiner concludes that it is "difficult to determine the applicability of the claimed method to any activity of any peptide" and the "trial and error e.g., exploratory studies do not provide an adequate description of the claimed invention." (OA at 7.)

Applicants respectfully traverse the rejection. An adequate written description requires that the specification convey to one having ordinary skill in the art that applicants were in possession of the claimed invention. Applicants respectfully submit that the specification adequately describes the claimed invention.

The Examiner states that terms such as "physical, chemical, biological and/or topological parameters" are broad descriptors in each of these parameters. Moreover, the Examiner states that the "activity," as used in the specification, includes all functions that peptides may exhibit. However, the breadth of the claim terms should not undermine the adequacy of the written description particularly when the skilled artisan would readily appreciate how each of the steps of the invention is intended to work. Instead, applicants contend that the Examiner must read the claims in view of the full content of the specification and the skill in the art, and not rely on

individual sentences to support the rejection. A person skilled in the art reading the full specification would appreciate that each of the claim-designated steps are fully and adequately described.

In fact, applicants respectfully direct the Examiner to Example 12 of the Written Description Guidelines, which provide an example of how a bioinformatics claim should be reviewed in view of the written description requirement. For the convenience of the Examiner, Example 12 is set forth below:

> **Example 12:** Bioinformatics
> **Specification:** The specification discloses a process for identifying and selecting biological compounds that are present in a biological system in a tissue specific manner. In the disclosed process the expression level of a set of compound is quantitatively determined in multiple tissues within an organism. The expression level data is then graphically displayed in such a manner that compounds are differentially expressed are easily identified. An artisan interested in identifying a compound that is expressed at a high level in one tissue and at a different level in a second tissue may easily select compounds that are expressed in a tissue specific manner based on the displayed information. The specification indicates that the compounds to be detected encompass DNA, RNA and proteins as well as metabolites. The specification does not provide any particular examples, but discloses that the expression levels can be determined by any analytical method consistent with the class of compounds being detected. This type of measurement requires actual physical steps.
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> **Claim:**
> A computer-implemented method of selecting tissue-specific compounds, said method comprising the steps of
> (a) analyzing the expression level of compounds in a first and second tissue and obtaining expression level data for each of said compounds;
> (b) inputting the expression level data obtained in step a) into a computer;
> (c) displaying a first axis corresponding to the expression level of each of said compounds in a said first tissue;
> (d) displaying a second axis substantially perpendicular to said first axis, said second axis corresponding to the expression level data of each of said compound in said second sample
> (e) displaying a mark at a position, wherein said position is selected relative to said first axis in accordance with an expression level of each of said compound in said first sample and relative to said second axis in accordance with the expression of said compound in said second sample; and
> (f) selecting a compound of interest on the position of the mark.
>
> **Analysis:**
> A review the full content of the specification indicates that obtaining, inputting, and displaying the expression level of compounds is essential to the operation of the claimed invention.
> A search of the prior art indicates that obtaining the expression level data of compounds is conventional in the art, and that data display devices and associated support algorithms are well known in the art.
> A review of the claim indicates that the claim is drawn to a generic environment for the display of compounds in a tissue specific manner.

> Since there is no species claimed or disclosed, the claim is analyzed as a claim drawn to a single embodiment. There is no actual reduction to practice of the claimed invention, or clear depiction of the claimed invention in detailed drawings. However, reading the specification in light of the knowledge and level of skill in the art, the specification discloses the complete steps of the claimed process. See In re Hayes Microcomputer Products Inc. Patent Litigation, 982 F2d. 1527, 1534-35, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992), where the court stated.
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> > One skilled in the art would know how to program a microprocessor to perform the necessary steps desired in the specification. Thus, an inventor is not required to describe every detail of his invention. An applicant's disclosure obligation varies according to the art to which the invention pertains.
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> In this fact situation, the art is sufficiently developed so as to put one of skill in the art in possession of the complete steps of the process. In other words, one skilled in the relevant art would understand what is intended by the claimed invention and know how to carry it out.
>
> **Conclusion:** There is adequate written description for what is claimed.

Similar to Example 12 of the Written Description Guidelines, the art is sufficiently developed in the instant claimed process so as to put one of skill in the art in possession of the complete steps of the process.

The claim is directed to a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The selection of a plurality of first test peptides to create a first test peptide library is conducted based on methodologies the user, as one skilled in the art, would readily appreciate. The method for making such libraries has been described in the art, for example, at page 16, lines 20-23. Space filling designs are known in the art and exemplary designs include full factorial designs, fractional factorial designs, maximum diversity libraries, genetic algorithms, coverage designs, spread designs, cluster based designs, Latin Hypercube Sampling, optimal designs, etc. as described at page 19-25. One skilled in the art would readily appreciate what a "space filling design" is intended to be and would be capable of practicing the step of selecting peptides using a space filling design within the scope of the claimed invention.

Furthermore, applicants submit that the desired "activity" and the "parameters" are decided by the user on a case-by-case basis. One skilled in the art practicing the claimed

invention would understand what types of "activity" and "parameters" would be available or desired by them. The claims are not intended to be limited to a specific activity or to specific parameters. Rather, the specification provides examples of suitable activities at page 17 (such as altered cell growth, level of transcription, translation, post-translational processing, intracellular transport, secretion, etc.) and suitable parameters at pages 27-29 (such as molecular weight, charge, isoelectric point, total dipole moment, isotropic surface area, electronic charge index, hydrophobicity, etc.). Applicants contend that reading the specification in view of the knowledge in the art, one skilled in the relevant art would understand and fully appreciate what activity is intended to be determined based on their own needs and what parameter values are available to them.

The method of determining the relationships between the parameters and indicia of activity is further described in the specification. For example, the specification describes the use of an equation that may describe the relationship between the activity and parameters. *See* page 30, lines 19-25. Alternatively, the relationship may be a quantitative structure-activity relationship (page 30, lines 26-28), conventional line-fitting algorithms (page 33, lines 9-32), or distance function relationships (*see* page 34). Nevertheless, the determination of the relationship is described in the specification particularly in view of the knowledge of the skilled artisan.

The Examiner asserts that the definitions in the specification are inconsistent or the claim terms are not art-recognized. However, there has been no showing as to how or why the definitions or claim terms are either inconsistent or not art-recognized. For example, the Examiner has not identified a single inconsistency with Applicants' use of the definitions provided in the specification. Likewise, the Examiner has not indicated either why certain claim

terms are not art-recognized, or how those claim terms are traditionally used in the art to show inconsistency.

As set forth above, one skilled in the art would clearly understand what these claim terms mean. Moreover, the Written Description Guidelines further provide that the "absence of definitions of details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, para. 1, for lack of adequate written description." (Written Description Guidelines at 4). Nevertheless, Applicants submit that the instant specification provides sufficient details to apprise the skilled artisan of the scope of the claims.

Applicants respectfully request withdrawal of the instant rejection, in view of the foregoing and the amendments to the claims.

IV. Rejection under 35 U.S.C. §112, second paragraph

By the present Amendment, Applicants have canceled claims 74 and 77-81, and added new claims 128-134 to better define the invention and address some of the issues raised in the Office Action. For example, the Office Action indicated that the claims did not identify what is intended to be claimed. The Office Action also indicated that the claims include terms that do not conform to the accepted meaning in the art, and cites language such as: space-filling design, indicia of peptide activity, whole molecule parameter, sequence specific parameter, etc. to support the rejection of indefiniteness

Applicants continue to disagree with the allegations made in the Office Action. The Office Action does not support the Examiner's refusal to accept definitions and examples set forth in the specification as a whole, as well as the actual invention being defined by the claims. Simply put, the Office Action simply has not set forth a prima facie case of indefiniteness under §112, second paragraph. The Federal Circuit has indicated that a claim is definite if the claim

reasonably apprises one skilled in the art of the use and scope of the invention, when read in light of the specification, and if the language is as precise as the subject matter permits.[1] Additionally, the MPEP specifically states that focus "during examination of claims for compliance with the requirement for definiteness ... is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available."[2] (Emphasis added).

In order to properly establish a rejection of indefiniteness, it must be shown that:

1. the claims have been interpreted in light of the specification;
2. the claims have been interpreted as one skilled in the art would interpret them; and
3. the limitations, or subject matter, in the claim do not reasonably define the invention.

The Office Action has provided no indication that the claims are being interpreted in light of the specification. Rather, the Office Action appears to suggest that the claims have been read in a vacuum by indicating that claim terms do not conform with accepted meaning in the art. Applicants have previously provided specific citations to the specification that support the claim language, yet the Examiner has refused to accept them.

Applicants again submits that all the terms used in the pending claims are either well-known in the art or are defined in the specification with sufficient clarity to allow one skilled in the art to understand the invention being claimed. For example, the term "space-filling design" is well-known in the art and intended to be construed broadly in light of the examples provided in the detailed description. Accordingly, space-filling design encompasses all such techniques known to those skilled in the art. As discussed in the detailed description, exemplary space-filling designs include, but are not limited to, full factorial designs, fractional factorial designs,

[1] Shatterproff Glass Corp. v. Libbey-Owens Ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), cert. dismissed, 474 U.S. 976 (1985).
[2] MPEP §2173.02.

maximum diversity libraries, genetic algorithms, coverage designs, spread design, cluster based designs, Latin Hypercube Sampling, and other optimal designs (e.g. D-Optimal), and the like. See, for example, page 19, line 15 to page 20, line 22. Accordingly, one skilled in the art would understand how to use space-filling design to select peptides for the first test peptide library.

Likewise, the term "indicia of peptide activity" is adequately described in the detailed description to allow one skilled in the art to practice the invention. As discussed in the detailed description, for example, the indicia of peptide activity is a property that can be measured using various methods known to those skilled in the art. Such methods include, but are not limited to, ELISAs, and/or labels capable of producing signals detectable by: spectrophotometry, x-ray diffraction or absorption, magnetism, enzymatic activity, chemiluminescence, fluorescence, and so forth. See, for example, page 18, lines 9-21. The term "whole molecule parameter" is a value that characterizes a molecule irrespective of the arrangement of its consecutive atoms or sub-units. For example, the specification defines a whole molecule parameter for a peptide as one that does not depend on the order or sequence of the amino acids in the peptide (page 28, lines 2-6). The detailed description also provides examples of whole molecule parameters. See page 28, lines 15-21 and page 51, lines 14-16. Accordingly, one skilled in the art would understand both the definition of a whole molecule parameter and how to identify additional values which satisfy the definition of a whole molecule parameter.

The detailed description defines a "sequence-specific parameter" as one that is dependent on the specific order or sequence of the consecutive atoms, or sub-units. See page 28, lines 11-12. Accordingly, one skilled in the art would understand what is meant by a sequence-specific parameter.

The detailed description indicates that the "test requirement" is a desired value against which the measured indicia of the activity are compared (See page 7, lines 10-24). For example, if the indicia being measured is fluorescence, then the test requirement would correspond to a desired fluorescence value or range. Likewise, if the indicia being measured is enzymatic activity, then the test requirement would correspond to a desired level, or range, of enzymatic activity. More importantly, one skilled in the art would recognize that the test requirement is a property that is set forth by a user on a case-by-case basis while practicing the invention. Consequently, the test requirement cannot be established until the invention is being practiced, and must be set by one practicing the invention based on the property he/she is attempting to isolate. Moreover, Applicants do not seek to claim 'test requirements' *per se*, but rather a method that includes a step in which users can specify a test requirement.

Next, the Office Action has provided no indication that the claims have been interpreted as one skilled in the art would interpret them. As previously stated, all the terms cited in the Office Action are defined, supported, and well-known in the art. In fact, there are various issued patents that use language similar to the pending claims to describe, for example, a whole molecule parameter.[3] Consequently, it cannot be concluded that one skilled in the art would not understand what is meant by such terms. Importantly, the claim terms alleged to be indefinite have been used consistently throughout the specification.

Finally, the Office Action has improperly interpreted the claimed invention, and concluded that the claims do not reasonably define the invention. The Office Action appears to suggest that the claims must identify a particular peptide or somehow specify an exact number of variations of the peptides. However, the claims are not intended to define a method for identifying specific peptide(s), nor does the specification provide any such suggestions. Rather,

[3] See e.g. U.S. Patents 6,610,256; 6,605,426; 6,448,012; and 5,492,802.

the claims define a methodology for assisting in the identification of peptides. Accordingly, the claimed invention seeks to provide users with an improved ability to identify peptides. The peptides identified are ultimately selected by the user, not the methodology of the claimed invention. It is the user practicing the invention who must decide which peptides are being identified or the activities being sought. Likewise, it is the user who must specify a satisfactory test requirement. As previously indicated, one skilled in the art would quickly appreciate the benefits of the claimed invention.

Neither the claims nor the specification provide the illusion that specific peptides and/or specific activities have been identified. As discussed in the "background" section of the application, previous attempts to improve culture media have largely relied on ad hoc, trial-and-error techniques. There was a lack of systematic and predictive methods for identifying components to improve cell performance in culture, as well as high throughput methods for identifying medium components. Therefore, one of the objects of the invention seeks to provide a more economical and rapid method of identifying compounds with desired activities, not to identify any specific compound or compounds. This is accomplished without the extensive trial-and-error techniques used in the past.

Based on the foregoing, Applicants respectfully submit that (1) the Office Action has not made a prima facie case of indefiniteness, and (2) the presently pending claims are in full compliance with the requirements of 35 U.S.C. §112, second paragraph. Withdrawal of this rejection is respectfully requested.

The cancellation of dependent claims 77-81 has rendered the respective rejections under 35 U.S.C. §112, second paragraph moot. Regarding the remaining claims, Applicants

respectfully request reconsideration and withdrawal of this rejection in view of newly presented claim 128, and further amendments made to the pending dependent claims (82-95 and 129).

On page 8 of the Office Action, the Examiner also asserts that claim 74 is indefinite, as there appeared to be a lack of nexus of the method steps. While the cancellation of claim 74 renders this particular ground of rejection moot, Applicants would like to clarify the invention defined by newly presented claim 128. More particularly, independent claim 128 has been carefully prepared to properly define the invention and provide a clear nexus between the various steps. Independent claim 128 defines a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The method includes the steps of:

> constructing a first test peptide library comprising a plurality of first test peptides by means of a space-filling design, wherein the length of said first test peptides comprises no greater than twenty amino acids, and wherein said first test peptides are characterized by a first parameter and a second parameter, said first parameter being a whole molecule parameter and said second parameter being a sequence-specific parameter;
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> determining an activity, having an indicia, of said plurality of first test peptides;
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> measuring the indicia of said activity of said plurality of first test peptides;
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> determining a relationship between said indicia of said activity, said first parameter, and said second parameter;
>
> calculating an estimated indicia for each first test peptide in said first test peptide library using said determined relationship;
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> setting a test requirement, based on a desired activity, having a test indicia range;
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> selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide is a first test peptide having an estimated first indicia that satisfies said test requirement;
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> determining the indicia of said at least one second test peptide; and
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> identifying at least one second test peptide having an indicia that satisfies said test requirement.

The method of claim 128 is intended to reduce the actual number of experiments performed (i.e., trial-and-error techniques) when screening peptides for a particular activity, while maximizing the number of candidate peptides that may potentially have a desired measure

of the activity. This is accomplished by first constructing a library that contains a plurality of first test peptides having a length of twenty amino acids. The first test peptides can be selected using a space filling design, as is well-known in the art and previously discussed. Additionally, the first test peptides are characterized by a first parameter (i.e., a whole molecule parameter), and a second parameter (i.e., a sequence-specific parameter). Next, the first test peptides are tested such that a first indicia can be determined for a desired activity. As previously discussed, the desired activity corresponds to a particular feature of interest to a user. This indicia is measured for each first test peptide. A relationship is then determined between the measured first indicia, the first parameter and the second parameter. As discussed in the detailed description, the relationship is preferably mathematical or otherwise quantitative in nature.

Once the relationship has been determined, an estimated first indicia is calculated for each candidate peptide using the determined relationship. More particularly, known values (i.e., the first and second parameters) from the candidate peptides are used in conjunction with the determined relationship in order to compute an estimated value for the first indicia. Next, the user sets a test requirement based on the desired activity. The test requirement is in the form of a range of test indicia values. These values correspond to a desired range that satisfy a criteria the user considers important. Next, a second test peptide library containing at least one candidate peptide is selected. Only candidate peptides having an estimated first indicia that satisfy the test requirement are selected to be in the second test peptide library. The user then tests the second test peptides in order to determine the actual first indicia. Finally, the user identifies at least one second test peptide that satisfies the test requirement.

The method defined by claim 128 advantageously reduces the amount of experimentation required to identify peptides having a desired indicia as discussed in the "Background" section of

the application. This reduction can directly translate to a reduction in time and costs associated with identifying such peptides. Additionally, users are able to generate a substantially large group of candidate peptides that could potentially have an indicia which satisfies the test requirement. The candidate peptides can be filtered to a smaller number of second test peptides that will actually be tested. Consequently, the number of actual experiments conducted can be significantly reduced.

Applicants respectfully submit that claim 128 provides sufficient nexus between various steps so as to allow one skilled in the art to practice the invention. Accordingly, the rejection under 35 U.S.C. §112, second paragraph should be withdrawn.

V. Rejections under 35 U.S.C. §102

Claims 74, 81, 87-90 and 94 stand rejected under 35 U.S.C. §102 as anticipated by Tenson. In support of this rejection, the Office Action provides citation to several passages that allegedly disclose various steps recited in the claims.

While the cancellation of claims 74 and 77-81 renders this ground of rejection moot, Applicants respectfully submit that claim 128 is patentable over the art of record. Claim 128 defines a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The method includes, in part, the steps of:

> ...
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> determining a relationship between said indicia of said activity, said first parameter, and said second parameter;
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> calculating an estimated indicia for each first test peptide in said first test peptide library using said determined relationship;
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> setting a test requirement, based on a desired activity, having a test indicia range;
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> selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide is a first test peptide having an estimated first indicia that satisfies said test requirement;
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> ...

As previously stated, the method of claim 128 is intended to reduce the actual number of experiments performed when screening peptides for a particular activity, while maximizing the number of candidate peptides that may potentially have a desired measure of the activity.

While the Office Action alleges that Tenson discloses all of the steps recited in claim 74, Applicants' review of the cited passages has not revealed any disclosure of the steps recited in claim 128. Tenson does not appear to disclose or suggest a method of identifying peptides with a desired activity, as set forth in claim 128. Rather, Tenson is concerned with the isolation of erythromycin-resistant clones from 21-codon and 5-codon random mini-gene plasmid libraries. Tenson uses 21-codon library primarily to determine the predominant size of erythromycin resistant peptides. A 5-codon library is used to show IPTG-dependence of erythromycin resistance. In contrast to the claimed invention, Tenson does not disclose specific steps such as, for example, the determination of a relationship between indicia and at least two parameters from a single library of peptides.

There is simply no disclosure in Tenson for the specific features recited in claim 128, including at least the steps of:

...

> determining a relationship between said indicia of said activity, said first parameter, and said second parameter;
>
> calculating an estimated indicia for each first test peptide in said first test peptide library using said determined relationship;
>
> setting a test requirement, based on a desired activity, having a test indicia range;
>
> selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide is a first test peptide having an estimated first indicia that satisfies said test requirement;

...

Applicants therefore respectfully submit that the claims of the present invention are not anticipated by Tenson, and respectfully requests withdrawal of the rejection under 35 U.S.C. §102.

Claims 76, 82-95, and 129 depend, either directly or indirectly, from claim 128 and are therefore believed allowable for at least the reasons set forth above with respect to claim 128. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

Claims 74, 81, 87-90 and 94 were rejected under 35 U.S.C. §102 as anticipated by Ostrem. In support of this rejection, the Office Action provides citation to several passages that allegedly disclosed various steps recited in the claims.

While the cancellation of claims 74 and 77-80 also renders this ground of rejection moot, Applicants further submit that claim 128 is patentable over Ostrem. As previously stated, claim 128 defines a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. The method of claim 128 is intended to reduce the actual number of experiments performed when screening peptides for a particular activity while maximizing the number of candidate peptides that may potentially have a desired measure of the activity.

The Office Action alleges that Ostrem discloses all of the steps recited in claim 74. Applicants' review of the cited passages, however, has not revealed any disclosure of various steps recited in claim 128. Ostrem does not appear to disclose, or even suggest, a method of identifying peptides with a desired activity, as set forth in claim 128. Ostrem discloses a library for screening of biotinylated factor Xa-SAP mixture added to library beads. Beads that showed a blue color were destained, stripped, and further screened with the factor Xa-SAP-inhibitor mixture. In contrast to the claimed invention, Ostrem does not disclose specific steps such as,

for example, the determination of a relationship between indicia and at least two parameters from a single library of peptides.

There is simply no disclosure or suggestion in Ostrem for the specific features recited in claim 128, including at least the steps of:

> determining a relationship between said indicia of said activity, said first parameter, and said second parameter;
>
> calculating an estimated indicia for each first test peptide in said first test peptide library using said determined relationship;
>
> setting a test requirement, based on a desired activity, having a test indicia range;
>
> selecting a second test peptide library comprising at least one second test peptide, wherein each second test peptide is a first test peptide having an estimated first indicia that satisfies said test requirement;

Applicants therefore respectfully submit that the claims of the present invention are not anticipated by Ostrem, and request withdrawal of the rejection under 35 U.S.C. §102.

Claims 76, 82-95, and 129 depend, either directly or indirectly, from claim 128 and are therefore believed allowable for at least the reasons set forth above with respect to claim 128. In addition, these claims each introduce novel elements that independently render them patentable over the art of record.

Claims 130-134 are newly presented for consideration. These claims also introduce various novel steps that are not shown or suggested by the art of record. These claims are therefore believed allowable over the art of record.

For all the foregoing reasons, Applicants respectfully submit that all of the pending claims (76, 82-95, and 128-134) are now in condition for allowance. The Examiner is respectfully requested to contact the undersigned, to schedule an interview if it is believed that such contact would further the examination of the present application.

CONCLUSION

Applicants respectfully submit that, as described above, the cited prior art does not show or suggest the steps recited in the claims. Applicants do not concede that the cited prior art shows any of the steps recited in the claims. However, Applicants have provided specific examples of steps in the claims that are clearly not present in the cited prior art.

Applicants wish to clarify for the record, if necessary, that the claims have been amended to expedite prosecution. Moreover, Applicants reserve the right to pursue the original subject matter recited in the present claims in a continuation application.

Any narrowing amendments made to the claims in the present Amendment are not to be construed as a surrender of any subject matter between the original claims and the present claims; rather merely Applicants' best attempt at providing one or more definitions of what is believed to be suitable patent protection. In addition, the present claims provide the intended scope of protection that Applicants are seeking for this application. Therefore, no estoppel should be presumed, and Applicants' claims are intended to include a scope of protection under the Doctrine of Equivalents.

For all the reasons advanced above, Applicants respectfully submit that the rejections have been overcome and should be withdrawn.

For all the reasons advanced above, Applicants respectfully submit that the Application is in condition for allowance, and that such action is earnestly solicited.

Restriction Requirement

Applicants provisionally elect Group I, claims 76, 83-95 and 128, with traverse. A restriction requirement is proper when (1) the inventions are independent or distinct as claimed; and (2) there is a serious burden on the Examiner. (MPEP §803, emphasis added). It is believed that the examination of all the pending claims, claims 76, 82-95, and 128-134 (Groups I, II, III, IV, and V) together, would not pose a serious burden upon the Examiner.

At the outset, the restriction requirement does not provide a basis as to why Group V, claim 134, is subject to restriction. The comments provided in the action provide that Groups I-IV are unrelated, but does not provide any basis as to why Group V, claim 134, should be restricted from the other groups. "Examiners must provide reasons and/or examples to support conclusions [in a restriction requirement]." MPEP 803. Therefore, at a minimum, applicants contend that Groups I and V should be examined together.

The Examiner restricted Groups I, II, III and IV as being unrelated because these groups allegedly are "different inventions, are drawn to different methods comprising different process steps, and employ different components." *See* Restriction Requirement at 3. The Examiner relies on MPEP 806.04 as the basis for the restriction. However, that section of MPEP 806.04 states that "[t]wo different combinations, not disclosed as capable of use together, having different modes of operation, different functions or different effects are independent." Each of the pending claims, on the other hand, is directed to a method of identifying a peptide with a desired activity having an indicia that satisfies a test requirement. Therefore, all of the claims are directed to the same utility. Moreover, the claims recite the same basic steps defining the core of the invention: constructing a first test peptide characterized by a first and second parameter (which can include identifying initial peptides and selecting a plurality of test peptides as set

forth in claim 130); measuring first indicia of a property; determining a relationship between the first parameter, second parameter, and the measured first indicia; calculating an estimated indicia; setting a test requirement; selecting a second test peptide library; measuring the indicia of at least one second test peptide; and identifying at least one second test peptide having an indicia that satisfies the test requirement. Where the claims of an application define the same essential characteristics of an invention, "restriction therebetween should never be required. This is because the claims are but different definitions of the same disclosed subject matter, varying in breadth or scope of definition." MPEP 806.03. Because each of the claims is directed to a method of identifying a peptide using the same basic steps, applicants respectfully submit that examination of these groups together would not place an undue on the examiner.

At the very least, the claims dependent from claim 128 should be examined with claim 128 in Group I because applicants have shown that the steps described in the dependent claims are capable of being used in the claimed method of identifying peptides in claim 128. Specifically, claims 129 and 82 further recite that, in the method of identifying a peptide according to claim 128, a space-filling design may be used to expand the first test peptide library to include the isomers of such peptides. Therefore, these further steps require the practice of the individual steps in independent claim 128. Consequently, claims 129 and 82 of Group II, dependent from claim 128, should be examined with Group I, claims 76, 83-95, and 128.

Reconsideration and examination of Groups I, II, III, IV, and V together is respectfully requested. If the Examiner disagrees, Applicants respectfully request that Groups I, II, and V, or Groups I and V be examined together.

Election of Species

Applicants provisionally elect, with traverse, coverage design as the space-filling design, molecular weight as the whole molecule parameter, hydrophobicity as the sequence-specific parameter, 5 for the length of the peptide (e.g., pentamers), and enhancement or inducement of biological activity as the activity. In Group I, claims 76, 83-86, 88, 90-91, 93, 94, 95, and 128 read on the elected species. In the event that the Examiner examines additional groups of invention with Group I, applicants note that the following claims would read on the elected species:

Group II -- claims 82 and 129

Group III -- claims 130 and 131

Group IV -- claims 132 and 133

Group V – claim 134

Applicants acknowledge that pursuant to MPEP 803.02, if the members of a Markush group are "sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions." MPEP 803.02. Applicants respectfully contend that an examination of each of the species would not be unduly burdensome on the Examiner. Nevertheless, upon the finding that the elected species is allowable over the prior art, applicants acknowledge that, under MPEP 803.02, examination would be extended to the additional non-elected species.

Attorney Docket No. (P3250) 6675.142US1 Serial No. 09/359,260

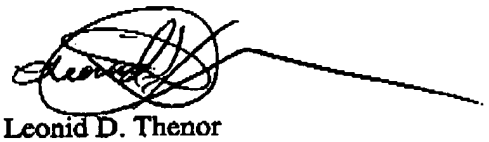
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment to deposit account no. 08-0219.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to deposit account no. 08-0219.

Respectfully Submitted,

Wilmer Cutler Pickering Hale and Dorr LLP



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